

AMENDMENTS TO THE CLAIMS

Prior to entry into national phase and examination of the instant application, please amend the claims of the application as follows:

1 – 30 (Canceled)

31. (Original) A pharmaceutical composition comprising a therapeutically effective amount of an antagonist/inhibitor of IL-1, or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt thereof and a therapeutically effective amount of IL-18BP or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt thereof.

32. (Original) The pharmaceutical composition according to claim 31, wherein the antagonist/inhibitor of IL-1 is IL-1Ra.

33. (Original) The pharmaceutical composition according to claim 32, wherein the IL-1Ra is Kineret.

34. (Original) A pharmaceutical composition comprising a therapeutically effective amount of an IL-1 antagonist/inhibitor or an expression vector comprising the coding sequence of IL-1 antagonist/inhibitor and IL-18BP or an expression vector comprising the coding sequence of IL-18BP.

35. (Original) A pharmaceutical composition comprising a therapeutically effective amount of an IL-1 antagonist/inhibitor or vector for inducing and/or enhancing the endogenous production of an IL-1 antagonist/inhibitor and IL-18BP or a vector for inducing and/or enhancing the endogenous production of IL-18BP in a cell.

36. (Original) A pharmaceutical composition comprising a therapeutically effective amount of an IL-1 antagonist/inhibitor or a cell that has been genetically modified to produce an IL-1 antagonist/inhibitor and IL-18BP or a cell that has been genetically modified to produce IL-18BP.

37. (Original) A method of treatment and/or prevention of inflammatory disease comprising administering to a host in need thereof an effective inhibiting amount of

IL-18BP, or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt thereof and an IL-1 antagonist/inhibitor or a mutein, functional derivative, fraction, circularly permuted derivative, fused protein, isoform and a salt thereof.

38. (Original) The method according to claim 37, wherein the antagonist/inhibitor of IL-1 is selected from caspase-1 (ICE) inhibitors, antibodies against IL-1, antibodies against any of the IL-1 receptor subunits, inhibitors of the IL-1 signaling pathway, antagonists of IL-1 which compete with IL-1 and block the IL-1 receptor, and IL-1 binding proteins, isoforms, muteins, fused proteins, functional derivatives, active fractions or circularly permuted derivatives thereof having essentially the same activity as an IL-1 binding protein.

39. (Original) The method according to claim 38, wherein IL-1 antagonist is IL-1Ra.

40. (Original) The method according to claim 39, wherein the IL-1Ra is Kineret.

41. (Currently amended) The method according to ~~claims 37 or 38~~ claim 37, wherein the antagonist/inhibitor is selected from, antisense mRNAs, soluble IL-1 receptors, and IL-1R antibody.

42. (Currently amended) The method according to any one of claims 37 to 41 or 67, wherein the IL-18BP is PEGylated.

43. (Currently amended) The method according to any one of claims 37 to 41 or 67, wherein the inhibitor of IL-18 is a fused protein comprising all or part of an IL-18BP fused to all or part of an immunoglobulin, and wherein the fused protein binds to IL-18.

44. (Original) The method according to claim 43, wherein the fused protein comprises all or part of the constant region of an immunoglobulin.

45. (Original) The method according to claim 44, wherein the immunoglobulin is of the IgG1 or IgG2 isotype.

46. (Currently amended) The method according to any one of claims ~~37 to~~
~~45~~ 37 to 41 or 67, wherein IL-18BP and the IL-1 antagonist/inhibitor are administered
simultaneously, or sequentially.

47. (Currently amended) The method according to any one of claims ~~37 to~~
~~46~~ 37 to 41 or 67, wherein IL-18BP is administered in an amount of about 0.0001 to 10
mg/kg of body weight, or about 0.01 to 5 mg/kg of body weight or about 0.1 to 3 mg/kg of
body weight or about 1 to 2 mg/kg of body weight.

48. (Currently amended) The method according to any one of claims ~~37 to~~
~~46~~ 37 to 41 or 67, wherein IL-18BP is administered in an amount of about 0.1 to 1000 mg/kg
of body weight or 1 to 100 mg/kg of body weight or about 10 to 50 mg/kg of body weight.

49. (Currently amended) The method according to any one of claims ~~37 to~~
~~48~~ 37 to 41 or 67, wherein the IL-1 antagonist/inhibitor is administered in an amount selected
from 0.0001 to 10 mg/kg or about 0.01 to 5 mg/kg or body weight, or about 0.01 to 5 mg/kg
of body weight or about 0.1 to 3 mg/kg of body weight or about 0.5 to 2 mg/kg of body
weight or about 1 mg/kg of body weight.

50. (Original) The method according to claim 49, wherein the IL-1
antagonist/inhibitor is administered at about 1 mg/kg of body weight.

51. (Currently amended) The method according to any one of claims ~~37 to~~
~~50~~ 37 to 41 or 67, wherein IL-18BP is administered subcutaneously.

52. (Currently amended) The method according to any one of claims ~~37 to~~
~~50~~ 37 to 41 or 67, wherein IL-18BP is administered intramuscularly.

53. (Currently amended) The method according to any one of claims ~~37 to~~
~~52~~ 37 to 41 or 67, wherein the IL-1 antagonist/inhibitor is administered subcutaneously.

54. (Currently amended) The method according to any one of claims ~~37 to~~
~~52~~ 37 to 41 or 67, wherein the IL-1 antagonist/inhibitor is administered intramuscularly.

55. (Currently amended) The method according to any one of claims ~~37 to 54~~ 37 to 41 or 67, wherein IL-18BP is administered daily.

56. (Currently amended) The method according to any one of claims ~~37 to 54~~ 37 to 41 or 67, wherein IL-18BP is administered three times per week.

57. (Currently amended) The method according to any one of claims ~~37 to 54~~ 37 to 41 or 67, wherein IL-18BP is administered once a week.

58. (Currently amended) The method according to any one of claims ~~37 to 57~~ 37 to 41 or 67, wherein the IL-1 antagonist/inhibitor is administered daily.

59. (Currently amended) The method according to any one of claims ~~37 to 57~~ 37 to 41 or 67, wherein the IL-1 antagonist/inhibitor is administered three times per week.

60. (Currently amended) The method according to any one of claims ~~37 to 57~~ 37 to 41 or 67, the IL-1 antagonist/inhibitor is administered once a week.

61. (Original) A method of treatment and/or prevention of inflammatory disease comprising administering to a host in need thereof an effective inhibiting amount an IL-1 antagonist/inhibitor or an expression vector comprising the coding sequence of IL-1 antagonist/inhibitor and IL-18BP or an expression vector comprising the coding sequence of IL-18BP.

62. (Original) The method of treatment and/or prevention according to claim 61 for gene therapy.

63. (Original) A method of treatment and/or prevention of an inflammatory disease comprising administering to a host in need thereof an effective inhibiting amount of an IL-1 antagonist/inhibitor or a vector for inducing and/or enhancing the endogenous production of an IL-1 antagonist/inhibitor and of an IL-18BP or a vector for inducing and/or enhancing the endogenous production of IL-18BP in a cell.

64. (Original) A method of treatment and/or prevention of an inflammatory disease comprising administering to a host in need thereof an effective inhibiting amount of IL-1 antagonist/inhibitor or a cell that has been genetically modified to produce an IL-1 antagonist/inhibitor and IL-18BP or a cell that has been genetically modified to produce IL-18BP.

65. (Original) The method according to any one of claims 61 to 64, wherein the inflammatory disease is selected from rheumatoid arthritis, allergy, asthma, systemic lupus erythematosus (SLE), IBD, septic shock, and osteoarthritis.

66. (Original) The method according to claim 65, wherein the inflammatory disease is rheumatoid arthritis.

67. (New) The method according to claim 38, wherein the antagonist/inhibitor is selected from, antisense mRNAs, soluble IL-1 receptors, and IL-1R antibody.